"Somatostatin," Brain peptide, Krieger et al., eds., John Wiley and Sons, New York, pp. 711-752 (1982); Gerich, "Somatostatin and analogues," Diabetes mellitus: Theory and practice, Ellenberg et al., eds., Medical Examinations, New York (1983); Wass, "Somatostatin," Endocrinology, DeGroot, ed., WB Saunders, Philadelphia, PA (1989); Patel, "General aspects of the biology and function of somatostatin," Basic and clinical aspects of neuroscience, Weil et al., eds., Springer-Verlag, Berlin (1992)). In neurons and cells, somatostatins are often co-localized with other factors (*e.g.*, norepinephrine, CCK, neuropeptide-Y, CGRP, GABA, VIP, substance P) (Gibbins, "Co-existence and co-function," The comparative physiology of regulatory peptides, Holmgren, ed., Chapman and Hall, London/New York (1989)).

Please replace the paragraph at page 7, line 5 to line 16, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, with notations to indicate the changes made.

Figure 5 compares the amino acid (lower left) and cDNA nucleotide (upper right) sequence identities vertebrate somatostatins. AF I denotes anglerfish (Hobart et al., Nature, 288, 137-141 (1980)), CF I denotes catfish I (Minth et al., J. Biol. Chem., 257, 10372-10377 (1982)), H denotes human (Shen et al., Proc. Natl. Acad. Sci. USA, 79, 4575-4579 (1982)), B denotes bovine (Su et al., Mol. Endocrinol., 2, 209-216 (1988)), M denotes monkey (Travis and Sutcliffe, Proc. Natl. Acad. Sci. USA, 85, 1696-1700(1988)), R denotes rat (Goodman et al., J. Biol. Chem., 258, 5570-5573 (1983)), C denotes chicken (Nata, GenBank direct submission, Accession No. X60191 (1991)), FR I denotes frog (Tostivint et al., Proc. Natl. Acad. Sci. USA, 93, 12605-12610 (1996)), TR II' denotes rainbow trout-II' (Moore et al., Gen. Comp. Endocrinol., 98, 253-261 (1995)), TR II" denotes rainbow trout-II", and TR I denotes rainbow trout-I.

Please replace the paragraph at page 7, line 17 to page 8, line 10, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, with notations to indicate the changes made.

Figure 6 aligns the deduced rainbow trout PPSS-I C-terminal region amino acid sequence to other PPSS-I C-terminal region amino acid sequences from other vertebrates. [a]Sequences arranged for maximum alignment; identity is greatest if it is assumed there has been a 2-amino acid deletion (designated by asterisks) from rainbow trout and bowfin (Wang et al., Regul. Peptides, 47, 33-39 (1993). [b]Putative peptide deduced from cDNA. [c]Peptide sequence deduced from cDNA and confirmed by processing analysis for anglerfish I (Hobart et al, Nature, 288, 137-141 (1980); Goodman et al., Proc. Natl. Acad. Sci. USA, 77, 5869-5873 (1980); Andrews and Dixon, Biochemistry, 26, 4853-4861 (1987)), catfish I (Andrews and Dixon, J. Biol. Chem., 256, 8267-8270 (1981); Minth et al., J. Biol. Chem., 257, 10372-10377 (1982)), and frog (Vaudry et al., Biochem. Biophys. Res. Commun., 188, 477-482 (1992); Tostivint et al., Proc. Natl. Acad. Sci. USA, 93, 12605-12610 (1996)). [d]Peptide sequence derived directly from analysis of isolates of islet extracts obtained from hagfish (Conlon et al., Endocrinology, 122, 1855-1859 (1988)), lamprey (Andrews et al., J. Biol. Chem., 263, 15809-15814 (1988)), torpedo (Conlon et al., Gen. Comp. Endocrinol., 60, 406-413 (1985)), ratfish (Conlon et al., Gen. Comp. Endocrinol., 80, 314-320 (1990)), sturgeon (Nishii et al., Gen. Comp. Endocrinol., 99, 6-12 (1995)), eel (Conlon et al., Endocrinology, 122, 1855-1859 (1988)), flounder and sculpin (Conlon et al., Eur. J. Biochem., 168, 647-652 (1987a)), salmon (Plisetskaya et al., Gen. Comp. Endocrinol., 63, 252-263 (1986)), salamander (Cavanaugh et al., Gen. Comp. Endocrinol., 101, 12-20 (1996)), pigeon (Spiess et al., Proc. Natl. Acad. Sci. USA, 76, 2974-2978 (1979)), alligator (Wang and Conlon, Peptides, 14, 573-579 (1993)), and ovine (28-amino acid form shown for purposes of comparison; Pradayrol et al., FEBS Lett., 109, 55-58 (1980)).

Please replace the paragraph at page 8, line 11 to line 32, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, with notations to indicate the changes made.

B4

Figure 7 aligns the deduced rainbow trout PPSS-I, PPSS-II' and PPSS-II" amino acid sequences with PPSSs of other vertebrates; sequence identity was maximized by inserting gaps (denoted by dashed lines); conserved amino acids are shaded. H denotes human (Shen et al., Proc. Natl. Acad. Sci. USA, 79, 4575-4579 (1982)); M denotes monkey (Travis and Sutcliffe, Proc. Natl. Acad. Sci. USA, 85, 1696-1700 (1988)); B denotes bovine (Su et al., Mol. Endocrinol., 2, 209-216 (1988)); R denotes rat (Goodman et al., J. Biol. Chem., 258, 570-573 (1983)); C denotes chicken (Nata, GenBank direct submission, Accession No. X60191 (1991)); FR I and FR II denote frog I and frog II (Tostivint et al., Proc. Natl. Acad. Sci. USA, 93, 12605-12610 (1996)); AF I denotes anglerfish I (Hobart et al., Nature, 288, 137-141 (1980)); AF II denotes anglerfish II (Goodman et al., Proc. Natl. Acad. Sci. USA, 77, 5869-5873 (1980); Goodman et al., Proc. Natl. Acad. Sci. USA, 79, 1682 (1982); Hobart et al., Nature, 288, 137-141 (1980)); CF I denotes catfish I (Minth et al., J. Biol. Chem., 257, 10372-10377 (1982)); CF II denotes catfish II (Fujita et al., Peptides, 2, 123-131 (1981)); GF I-III denotes goldfish I-III (Lin et al., Endocrinology, 140, 2089-2099 (1999)); TRI denotes trout I; TRII' denotes trout II' (Moore et al., Gen. Comp. Endocrinol., 98, 253-261 (1995)); and TRII" denotes trout II".

Please replace the paragraph at page 12, line 22 to page 13, line 8, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, with notations to indicate the changes made.

B5

Percent identity is determined by aligning the residues of the two amino acid or nucleotide sequences to optimize the number of identical amino acids or nucleotides along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of identical amino acids or nucleotides, although the amino acids or nucleotides in each sequence must nonetheless remain in their proper order. Preferably, two amino acid sequences are compared using the Blastp program, version 2.0.9, of the BLAST 2 search algorithm, as described by Tatusova et al. (*FEMS Microbiol. Lett.*, 174, 247-250 (1999)), and available at <http://www.ncbi.nlm.nih.gov/blast/>. Preferably, the default values for all BLAST 2 search parameters are used, including matrix = BLOSUM62; open gap penalty = 11, extension gap penalty = 1, gap x_dropoff = 50, expect = 10, wordsize = 3, and filter on. Likewise, two nucleotide sequences are compared using the Blastn program, version 2.0.11, of the BLAST 2 search algorithm, also as described by Tatusova et al. (*FEMS Microbiol Lett*, 174, 247-250 (1999)), and available at <http://www.ncbi.nlm.nih.gov/blast/>. Preferably, the default values for all BLAST 2 search parameters are used, including reward for match = 1, penalty for mismatch = -2, open gap penalty = 5, extension gap penalty = 2, gap x_dropoff = 50, expect = 10, wordsize = 11, and filter on.

Please replace the paragraph at page 26, line 17 to line 26, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, with notations to indicate the changes made.

B6

Oligonucleotides were either custom synthesized by National Biosciences (Plymouth, MN) or supplied with Gibco/BRL 3'- and 5'-RACE kits. Oligonucleotides used as probes were 5'-end labeled with [γ^{32}P]-ATP (Amersham) using T4-polynucleotide kinase (Promega) as previously described in Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd Edition, Plainview, New York, Cold Spring Harbor

B6 Cont'd

Laboratory Press (1989). The full-length SS-II cDNA probe was radiolabeled with [α^{32}P]-CTP by random priming (Prime-a-Gene; Promega) according to the manufacturer's protocol. All radiolabeled probes were purified over Elutip-D columns (Schleicher and Schuell) according to the manufacturer's protocol.

Please replace the paragraph at page 30, line 7 to line 22, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, with notations to indicate the changes made.

B7

The deduced PPSS-II' (SEQ ID NO:9) and PPSS-II" (SEQ ID NO:15) proteins in rainbow trout Brockmann bodies contain 115 and 111 amino acids, respectively, both slightly shorter than the precursors of anglerfish (Goodman et al., J. Biol. Chem., 258, 570-573 (1983); Goodman et al., Proc. Natl. Acad. Sci. USA, 77, 5869-5873 (1980); and Hobart et al., Nature, 288, 137-141 (1980)), and goldfish (Lin et al., Endocrinology, 140, 2089-2099 (1999)), the only other known PPSS-IIs containing [Tyr^7, Gly^{10}]-SS-14. Rainbow trout PPSS-II' shared 43.5 % amino acid identity with anglerfish PPSS-II and 51.3 % amino acid identity with goldfish PPSS-II. The amino acid identity between rainbow trout PPSS-II" and anglerfish PPSS-II was 38.7 % while the identity between trout PPSS-II" and goldfish PPSS-II was 41.4%. Amino acid identities between rainbow trout PPSS-IIs and precursors derived from gene 1 were lower, between 37.9 % and 22.5 %. Rainbow trout PPSS-IIs were least similar to the preprosomatostatin giving rise to catfish SS-22. Although the evidence is limited, it appears that evolutionary selection has acted to conserve the biologically active C-terminal domain of PPSSs (see Fig. 7).

Please replace the paragraph at page 35, line 17 to page 36, line 4, with the following rewritten paragraph. Per 37 C.F.R §1.121, this paragraph is also shown in Appendix A, with notations to indicate the changes made.

B8

The present study revealed that two PPSS-II mRNAs of rainbow trout are differentially expressed. This conclusion is based on several observations. First, the pattern of PPSS-II' mRNA and PPSS-II" mRNA is tissue-specific. For example, only PPSS-II" mRNA was detected in the brain of rainbow trout, whereas both PPSS-II' and PPSS-II" mRNA were detected in pancreas and various regions of the gut. Brain-specific expression of the mRNA encoding the alternate form of SS in frogs (denoted PSS2) (Tostivint et al., Proc. Natl. Acad. Sci. USA, 93, 12605-12610 (1996)) and cortistatin (de Lecea et al., Nature, 381, 242-245 (1996)) also has been reported. Previous immunocytochemical studies support a similar distribution of [Tyr^7,Gly^{10}]-somatostatin-14-containing peptides in the intestine (Beorlegui et al., Gen. Comp. Endocrinol., 86, 483-495 (1992)) and stomach (Barrenechea et al., Tissue Cell, 26, 309-321 (1994)) of rainbow trout. Second, the abundance of PPSS-II mRNAs was different with specific tissues. Within the Brockmann body of rainbow trout, the predominant message form was that encoding for PPSS-II", whereas in the stomach the predominant form was that encoding PPSS-II'. Lastly, the pattern of PPSS-II expression within the endocrine pancreas of rainbow trout was modulated by nutritional state. Together, these results suggest that rainbow trout produce two forms of gene 2 SS peptides and that there exists mechanisms to independently regulate the expression of each.